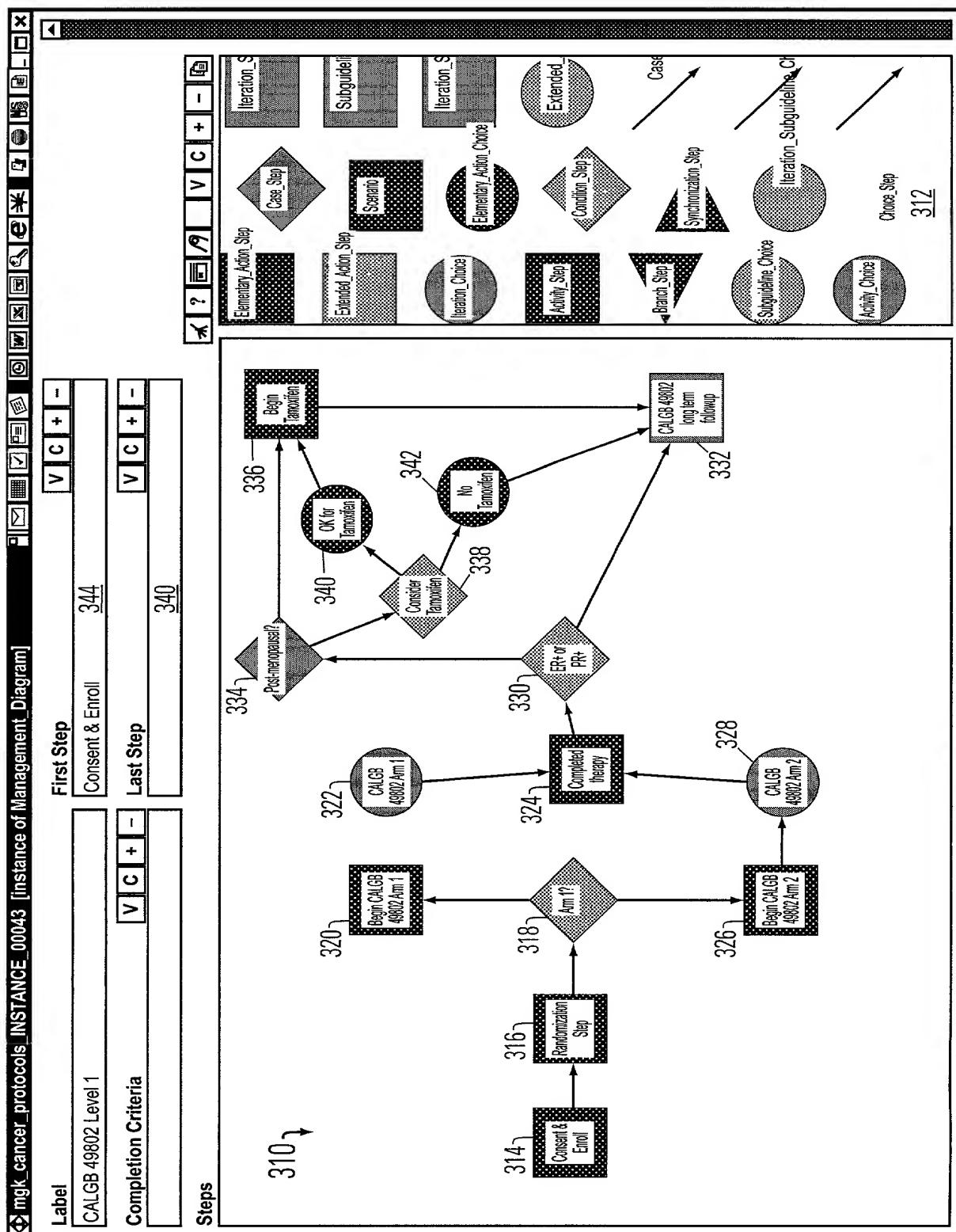
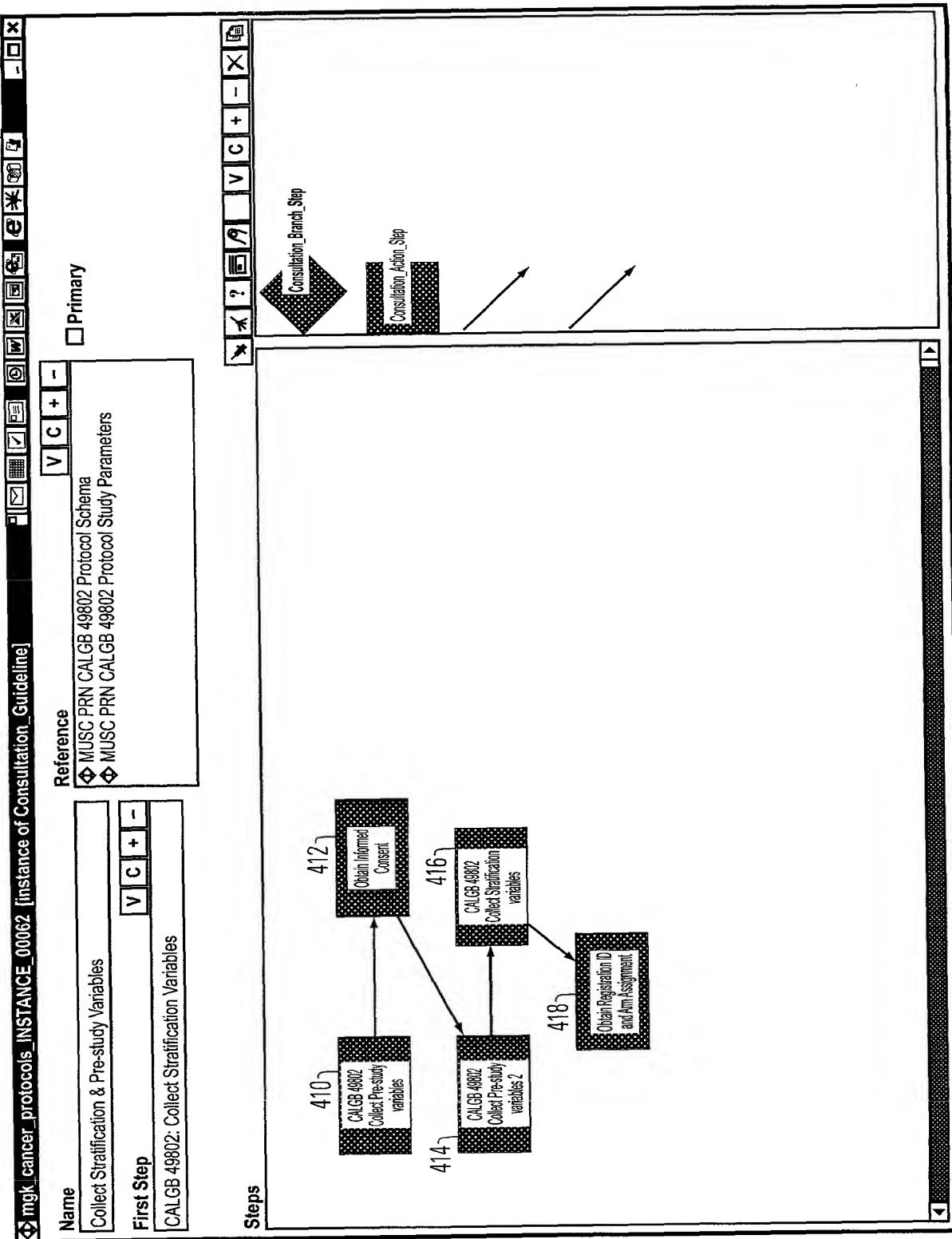


Cancer_protocols_INSTANCE_00039 [Instance of Cancer_Clinical_Protocol]	
Label	CALGB 49802
Version	mgk 25Jan00
Title	Phase III Study of Adriamycin/Taxotere vs Adriamycin/Cytoxan for the Adjuvant treatment of Node Positive or High Risk Node Negative Breast Cancer
Authors	M. G. Public
Reference	<input type="checkbox"/> V <input type="checkbox"/> C <input checked="" type="checkbox"/> + <input type="checkbox"/> - <input checked="" type="checkbox"/> MUSC PRN web page
Clinical Algorithm	<input type="checkbox"/> V <input type="checkbox"/> C <input checked="" type="checkbox"/> + <input type="checkbox"/> - CALGB 49802 Level 1
Context Reference	<input type="checkbox"/> V <input type="checkbox"/> C <input checked="" type="checkbox"/> + <input type="checkbox"/> - [Empty]
Entry Criteria (1 values)	
Protocol Name	CALGB 49802
Clinical State Name	[Empty]
Inclusion List	
<input type="checkbox"/> Histologically or cytologically confirmed invasive breast cancer <input type="checkbox"/> 1-3 histologically involved axillary lymph nodes <input type="checkbox"/> No evidence of metastatic disease (M0) <input type="checkbox"/> Absolute neutrophil count of at least 1,500/mm ³ <input type="checkbox"/> Platelet count of at least 100,000/mm ³ <input type="checkbox"/> Left ventricular ejection fraction at rest at least 45% by MUGA <input type="checkbox"/> Bilirubin no greater than 1.2 times upper limit of normal (ULN)	
Exclusion List	
<input type="checkbox"/> Tumor of any size with direct extension to chest wall or skin (T4) <input type="checkbox"/> Patient is pregnant or nursing	
212	
210	



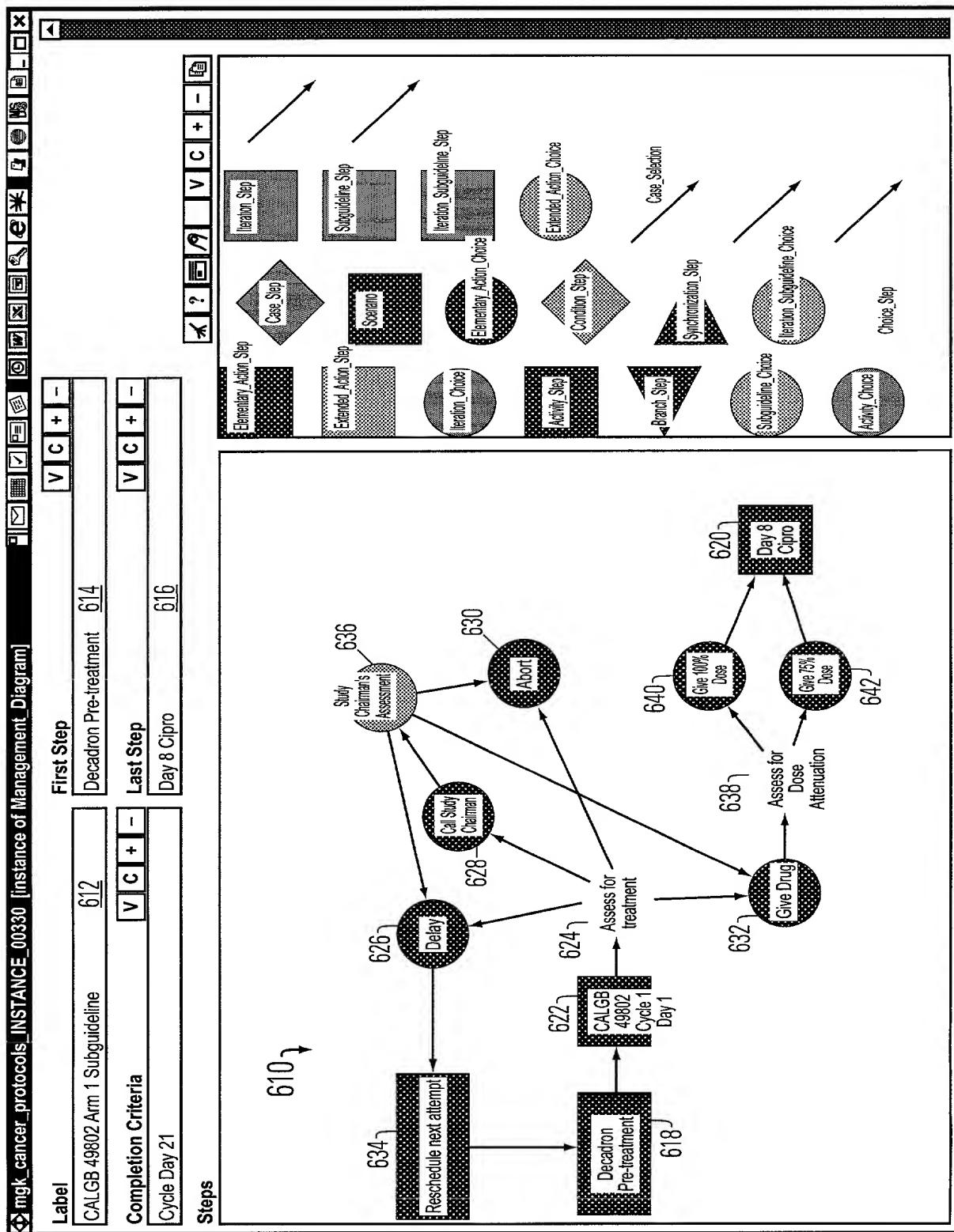


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mgk_cancer_protocols_INSTANCE_00063 [instance of Consultation_Act...]

Label	mgk_cancer_protocols_INSTANCE_00063 [instance of Consultation_Act...]			
CALGB 49802: Collect Stratification Variables	<input type="checkbox"/> Evaluate lymph node status <input type="checkbox"/> Evaluate menopausal status <input type="checkbox"/> Evaluate estrogen receptor status <input type="checkbox"/> Evaluate progesterone receptor status			
Followed By	<input type="checkbox"/> V	<input type="checkbox"/> C	<input type="checkbox"/> +	<input type="checkbox"/> -
Rule In	<input type="checkbox"/> V	<input type="checkbox"/> C	<input type="checkbox"/> +	<input type="checkbox"/> -
Rule Out	<input type="checkbox"/> V	<input type="checkbox"/> C	<input type="checkbox"/> +	<input type="checkbox"/> -
References	<input type="checkbox"/> V	<input type="checkbox"/> C	<input type="checkbox"/> +	<input type="checkbox"/> -

FIG. 5



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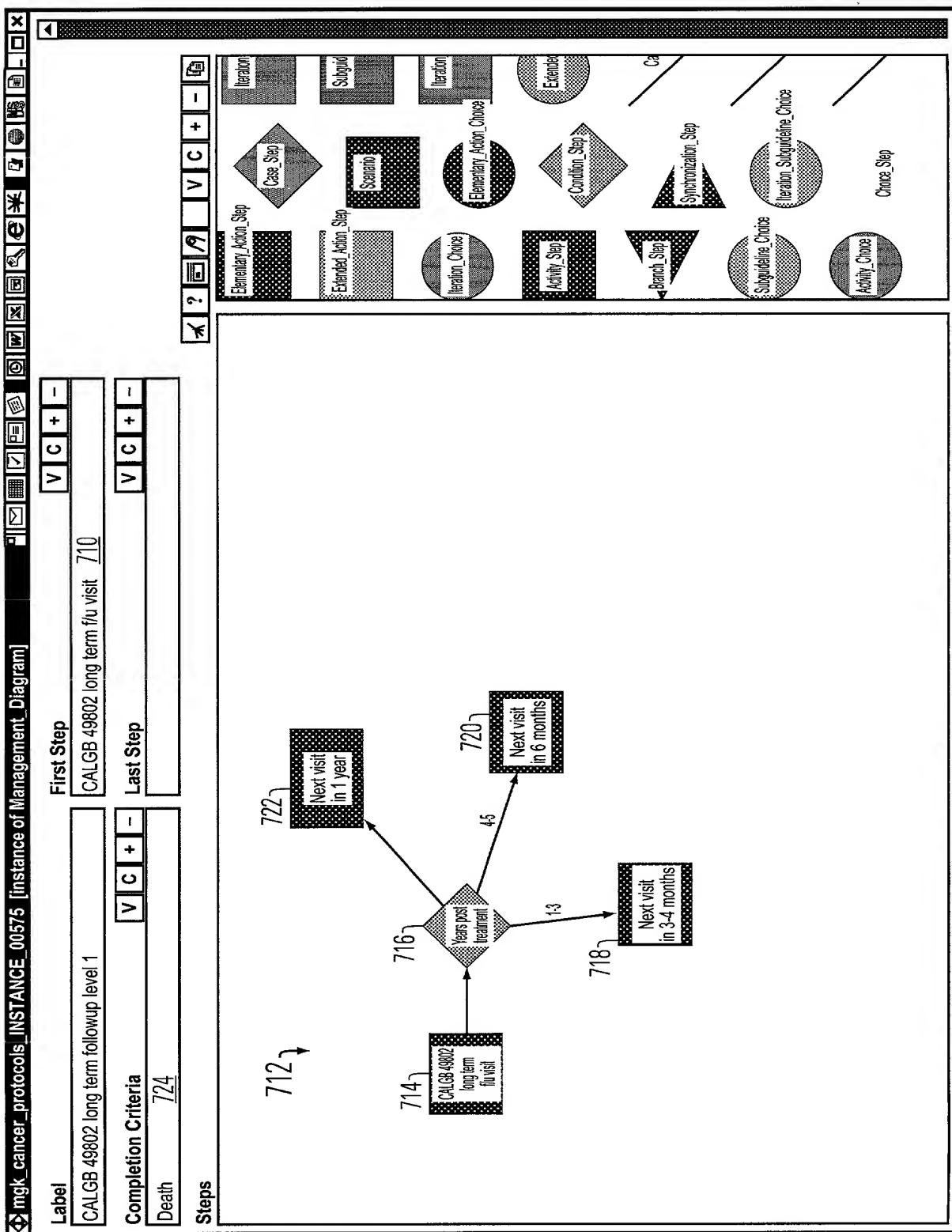


FIG. 7

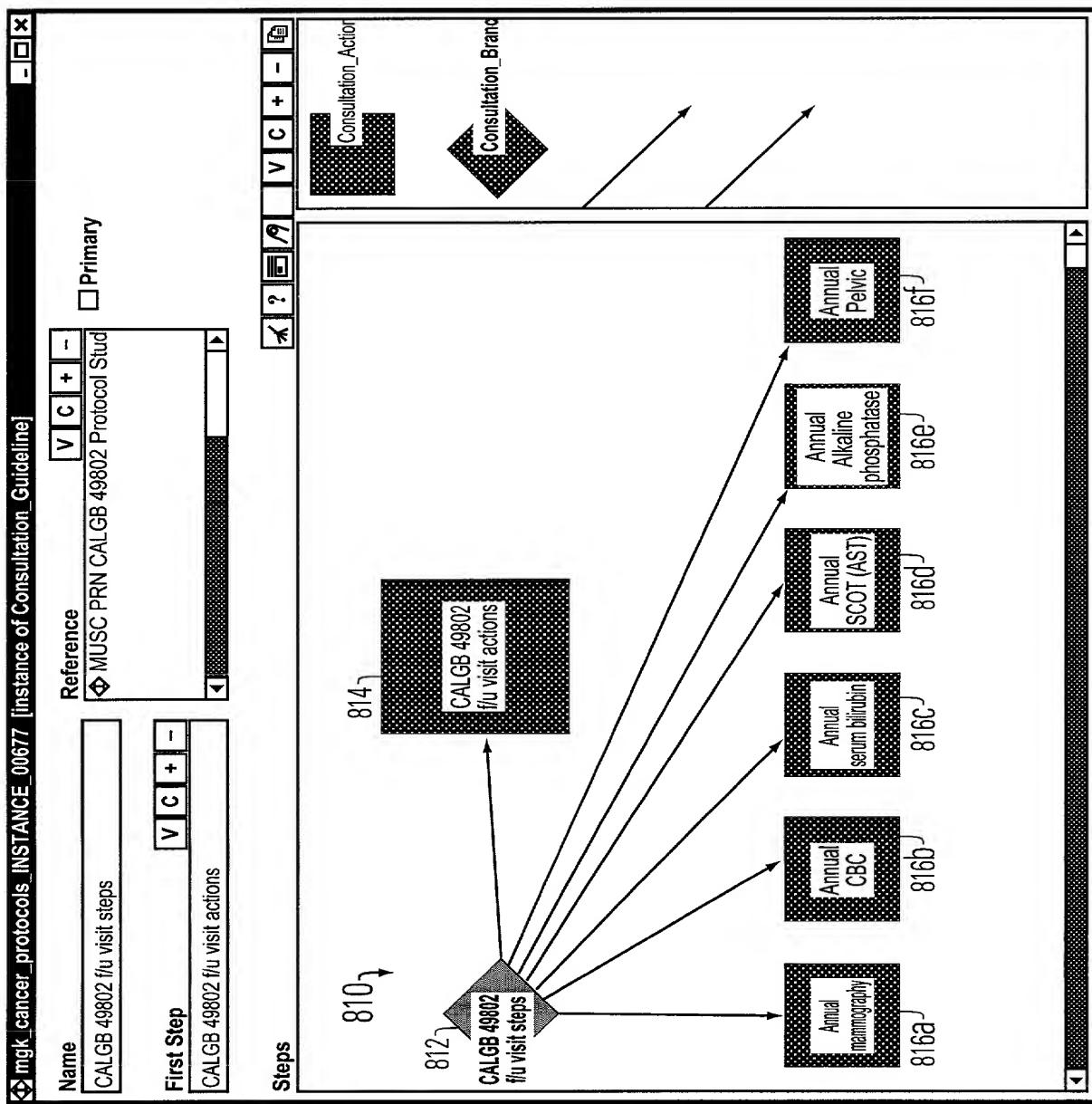
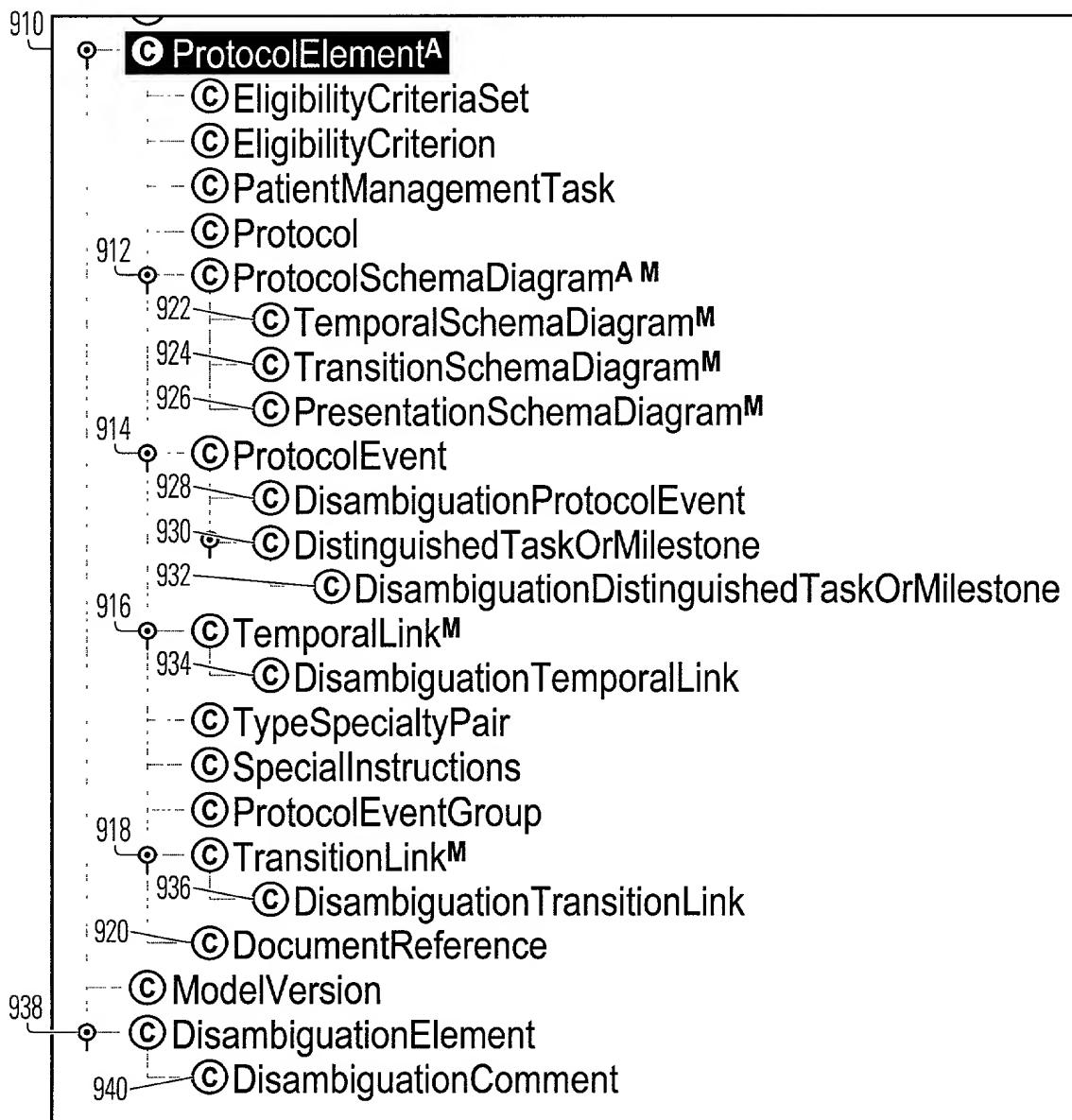


FIG. 8



10/41

910

© ProtocolElement

Name	ProtocolElement	Documentation	Constraints
Role	Abstract ^A	The superclass for all objects in the FastTrack protocol model.	<input type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Template Slots		<input type="checkbox"/> <input checked="" type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
Name	Type	Cardinality	Other Facets
1010 <input checked="" type="checkbox"/> disambiguationComments	Instance	multiple	classes={DisambiguationComment}
1011 <input checked="" type="checkbox"/> drillDown	Boolean	single	default={false}
1012 <input checked="" type="checkbox"/> encodingComments	String	single	
1013 <input checked="" type="checkbox"/> longDescription	String	single	
1014 <input checked="" type="checkbox"/> shortDescription	String	required single	

FIG. 10

The screenshot shows the Protégé 4.3.0 interface with the following details:

- Project Bar:** FastTrack Protocol Protégé-2000 [C:\My Documents\Latest FastTrack RDF + CALGB 9840\FastTrack Protocol.pprj]
- Relationship Bar:** Subclass ▶ V C X
- Class Hierarchy (Left):** Shows the class hierarchy for 'Protocol'. 'Protocol' is a subclass of 'THING' and 'SYSTEM-CLASS-A'. It has subclasses: 'ProtocolElementA' (1112), 'EligibilityCriteriaSet' (1124), 'EligibilityCriterion' (1125), 'PatientManagementTask' (1130), 'ProtocolSchemaDiagram' (116), 'ProtocolTitle' (117), 'QuickScreenCriterion' (1120), 'rdfs:isDefinedBy' (1128), 'rdfs:seeAlso' (1129), 'resource uri' (1131), 'shortDescription' (1132), 'siteAccrualTarget' (1133), 'siteLongDescription' (1134), 'siteShortDescription' (1135), 'sponsor' (1136), 'sponsorAccrualTarget' (1137), 'studyChair' (1138), 'trialPhase' (1139), and 'trialStatus' (1140). 'ProtocolElementA' is a subclass of 'Visit' (1120) and 'WeightedPath' (1152). 'Visit' is a subclass of 'VisitToVisitTransition' (1128). 'VisitToVisitTransition' is a subclass of 'DiseaseArea' (1150). 'DiseaseArea' is a subclass of 'CAM' (1150). 'CAM' is a subclass of 'ApplicationArea' (1152). 'ApplicationArea' is a subclass of 'Visitcycle' (1154). 'Visitcycle' is a subclass of 'DiseaseA' (1110), 'DiseaseQualifiersA' (1110), and 'ModelVersion' (1110).
- Class Details (Right):** The 'Protocol' class is shown as an instance of 'rdfs:Class'. It has the following properties:
 - Name:** Protocol
 - Documentation:** The document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol also usually gives the background and
 - Template Slots:** A table showing slots and their values:

Name	Type	Cardinality	Default	Other Facets
ProtocolSchemaDiagram	Instance	Single		classes=[ProtocolSchemaDiagram]
ProtocolTitle	String	Single		values=[Prostate Cancer, Colorectal Cancer, Breast Cancer]
QuickScreenCriterion	Symbol	Single		1122 classes=[URI, rdfs:Resource]
rdfs:isDefinedBy	Instance	Single		1122 classes=[URI, rdfs:Resource]
rdfs:seeAlso	Instance	Single		classes=[URI]
resource uri	String	Single		
shortDescription	String	Single		
siteAccrualTarget	String	Single		
siteLongDescription	String	Single		
siteShortDescription	String	Single		
sponsor	String	Single		
sponsorAccrualTarget	String	Single		
studyChair	Symbol	Single		
trialPhase	Symbol	Single		values=[Phase I, Phase II, Phase III, Phase IV, Phase V, Phase VI]
trialStatus	Symbol	Single		values=[On Hold, Terminated, Active]
 - Superclasses:** ProtocolElementA
 - Subclasses:** None

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1210

FastTrack Protocol_INSTANCE_00212 [instance of Protocol]

ProtocolTitle	Version
A Phase III Study of Paclitaxel via Weekly 1-Hour Infusion v	Update #1
ProtocolIdentifier	VersionDate
CALGB 9840	December 15, 1998
OfficialSourceDocument	EligibilityCriteriaSet
http://prn.musc.edu/research/protocol/deptmed/divhonz/bi	<input type="button" value="V"/> <input type="button" value="C"/> <input type="button" value="+"/> <input type="button" value="-"/>
ShortDescription	1212
CALGB 9840	◆ CALGB 9840 Eligibility Criteria
StudyChair	
Andrew D. Seidman, M.D.	
Sponsor	LongDescription
CALGB	
QuickScreenCriterion	
Breast Cancer	
Sponsor	
To compare "standard" (S) paclitaxel at 175 mg/m ² via 3-hour infusion every 3 weeks to "dose-dense" (DD) paclitaxel at 80 mg/m ² via 1-hour infusion every week	
TrialStatus	AccrualStatus
Active	Open for accrual
TrialPhase	TrialType
Phase III	Cooperative group
FirstVisit	ProtocolSchemaDiagram
Screening Visit	<input type="button" value="V"/> <input type="button" value="C"/> <input type="button" value="+"/> <input type="button" value="-"/>
	1214
	CALGB 9840 Schema

FIG. 12

914

© ProtocolEvent

Name	Documentation		
ProtocolEvent	This class is used to represent a single patient visit during the course of a clinical protocol.		
Role	Constraints		
Concrete	C		
Template Slots			
Name	Type	Cardinality	Other Facets
1010 <input type="checkbox"/> disambiguationComments	Instance	multiple	classes={DisambiguationComment}
<input type="checkbox"/> drillDown	Boolean	single	default={false}
<input type="checkbox"/> encodingComments	String	single	
1312 <input type="checkbox"/> eventType <input type="radio"/>	Symbol	single	allowed-values={Screening,Treatme...}
<input type="checkbox"/> incomingLinks <input type="checkbox"/>	Instance	multiple	classes={TemporalLink}
1012 <input type="checkbox"/> isMilestone <input type="radio"/>	Boolean	single	default={false}
1310 <input type="checkbox"/> longDescription	String	single	
1314 <input type="checkbox"/> managementTasks	Instance	multiple	classes={PatientManagementTask}
1014 <input type="checkbox"/> outgoingLinks <input type="checkbox"/>	Instance	multiple	classes={TemporalLink}
<input type="checkbox"/> shortDescription	String	required single	

FIG. 13

2 day f/u for Visit 1 (DisambiguationProtocolEvent)

ShortDescription 2 day f/u for Visit 1	EventType Treatment
LongDescription These labs must be obtained in the morning.	
Incoming Links Visit 1 to Visit 1 f/u	Management Tasks V C + - Phone F/U Creatinine Ionized Ca Mg PO4 CBC with Diff and plt
OutgoingLinks	EncodingComments
DisambiguationComments Inconsistent tasks in tx plan and assessment 1410	

15/41

916

© TemporalLink (Connector_Metaclass)

Name	Constraints	C	+	~	Documentation
TemporalLink					This class a temporal constraint or anchoring between two visits.
Role	Concrete				
Template Slots					[v] [v] [c] [x] [+/-]
1010	Name	Type	Cardinality	Other Facets	
510	[S] disambiguationComments	Instance	multiple	classes={DisambiguationComment}	
1012	[S] dominant	Boolean	single	default={false}	
1518	[S] drillDown	Boolean	single	default={false}	
1516	[S] encodingComments	String	single		
1522	[S] first_object ^{o1}	Instance	single	classes={ProtocolEvent}	
1520	[S] longDescription	String	single		
1512	[S] maximumRelativeOffset	Integer	single		
1014	[S] minimumRelativeOffset	Integer	single		
	[S] offsetUnits	Symbol	required single	allowed-values={Years,Months,Week...}	
	[S] preferredRelativeOffset	Integer	single		
	[S] second_object ^{o2}	Instance	single	classes={ProtocolEvent}	
	[S] shortDescription	String	required single		

FIG. 15

Screening to Rheumatoid Factor (TemporalLink)

ShortDescription	FromEvent (first_object)	V C + -
Screening to Rheumatoid Factor	Screening	
preferredRelativeOffset	ToEvent (second_object)	V C + -
	Rheumatoid Factor	
MinimumRelativeOffset	DisambiguationComments	V C + -
-180		
MaximumRelativeOffset		
-1		
OffsetUnits	EncodingComments	
Days		
<input type="checkbox"/> Dominant		

FIG. 16

FastTrack Protocol Protégé-2000 [C:\My Documents\Latest FastTrack RDF + CALGB 9840\FastTrack Protocol.ppr]

Project Edit Window Help

Relationship: Subclass ▶ V C X

© Classes Forms Instances

© Visit (Instance of rdfs:Class)

Name Visit

Role Concrete ▶

Constraints V C + -

Documentation

An actual encounter between the provider and a patient on study. A number of possible visits are associated with a study (Protocol).

V C + -

Template Slots

Name	Type	Cardinality	Default	Other Facts
\$dataManagementTasks	1/16	Instance	Multiple	classes=[ManagementTask]
\$longDescription	String	Single		classes=[VisitToVisitTransition]
\$patientManagementTasks	Instance	Multiple		classes=[URl,rdfs:Resource]
\$possibleVisitTransitions	1/14	Instance	Single	classes=[URl,rdfs:Resource]
\$rdfs:isDefinedBy	1/12	Instance	Single	classes=[URl]
\$rdfs:seeAlso				
\$resourceUri	String	Single		
\$shortDescription	String	Single		
\$siteLongDescription	String	Single		
\$siteShortDescription	String	Single		

Rdfs:isDefinedBy

Rdfs:seeAlso

Resource Uri

Superclasses + -

© FastTrackClass

66 ↳ V + -

1710

<p>FastTrack Protocol INSTANCE_00014 [instance of Visit]</p> <p>ShortDescription</p> <p>Arm A Treatment Visit</p>	<p>PossibleVisitTransitions</p> <p>V C + -</p> <ul style="list-style-type: none">◊ Arm A Treatment to Arm A Treatment Retry #1 <u>1818</u>◊ Arm A Treatment to Long Term Followup <u>1818</u>◊ Arm A Treatment Visit to Arm A Treatment Visit <u>1810</u>	<p>PatientManagementTasks</p> <p>V C + -</p> <ul style="list-style-type: none">◊ Confirm granulocytes $\geq 13000 / \mu l$◊ Confirm no G-CSF given in past 24 hours◊ Give Dexmethosone 10 mg IV, 30 minutes◊ Give Diphenhydramine 50 mg IV, 30 minutes◊ Give Cimetidine 300 mg IV, 30 minutes◊ Give anti-emetics (*)◊ Give Arm A Paclitaxel treatment <u>1816</u>◊ Give G-CSF (*)◊ Evaluate Patient Response <u>1812</u>◊ Schedule next visit <u>1814</u>	<p>DataManagementTasks</p> <p>V C + -</p> <ul style="list-style-type: none">◊ Submit Form C-116 <u>1818</u>◊ Submit Form C-118 <u>1818</u>◊ Submit Form C-080◊ Submit Form C-344 + Form C-080 (*)◊ Submit Form C-344 + Form C-272 (*)◊ Submit Form C-113 (*)◊ Submit Form C-260 (*)◊ Submit Form C-300 (*)	<p>LongDescription</p> <p>Arm A of the CALG 9840 consists of treatment with Paclitaxel 175 mg/m² administered as a 3 hour infusion intravenously every three weeks. One cycle is equivalent to one infusion. Treatment cycles will be repeated every 21 days as long as the patient has stable or responding disease. Granulocyte count must be $\geq 1500/\mu l$ and platelet count must be $\geq 100,000/\mu l$ on day 1 of each cycle. Patients should receive a minimum of two cycles of therapy, unless there is rapid disease progression (>50% increase in product of bi-dimensional measurements).</p>	<p>SiteLongDescription</p> <p> </p>	<p>SiteShortDescription</p> <p> </p>
--------------------------------------------------------------------------------------------------------------------------	--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	--------------------------------------------	---------------------------------------------

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FastTrack Protocol Protégé-2000 [C:\My Documents\latest FastTrack RDF + CALGB 9840\FastTrack Protocol.ppr]

Project Edit Window Help

Relationship: Subclass ▶ V C X

Classes Forms Instances

© THING^A

- © .SYSTEM-CLASS^A
- © Diagram_Entity
- © Date
- © ProtocolElement^A — 1112
- © EligibilityCriteriaSet — 1124
- © EligibilityCriterion
- © PatientManagementTask — 1130
- © Protocol — 1116
- © ProtocolSchemaDiagram^M — 1132
- © Visit — 1128
- © VisitToVisitTransition^M
- © DiseaseArea
- © Amt
- © WeightedPath
- © ApplicationArea
- © VisitCycle
- © Disease^A
- © DiseaseQualifiers^A
- © ModelVersion

1110

© ManagementTask (instance of rdfs:Class)

Name	Constraints	V	C	+	-
ManagementTask					
Role					
Concrete					

Template Slots

Name	Type	Cardinality	Default	Other Facets
S.longDescription	Symbol	Single		values=[Medium,High,Low]
S.longDescription	String	Single		classes=[URI,rdfs:Resource]
S.rdfs.isDefinedBy	Instance	Single		classes=[URI,rdfs:Resource]
S.seeAlso	Instance	Single		classes=[URI]
S.resource uri	String	Single		
S.shortDescription	String	Single		
S.siteLongDescription	String	Single		
S.siteShortDescription	String	Single		

Documentation

A task related to this visit. Includes:
 checks that tasks prior to this visit occurred, ok's that tasks performed during this visit were done, or reminders for tasks to perform before

V C + -

Rdfs:isDefinedBy

Rdfs:seeAlso

Resource Uri

Superclasses

© FastTrackClass

1910

FIG. 19

FastTrack Protocol INSTANCE_002016 [instance of ManagementTask]

ShortDescription
Give Arm A Paclitaxel treatment

LongDescription

Give Paclitaxel 175 mg/m² IV, 3 hours. This treatment is given to patients in Arm A of the CALGB 9840 protocol. It is given once every 3 weeks. One cycle is equivalent to one infusion. Granulocyte count must be $\geq 1500/\mu\text{l}$ and platelet count must be $\geq 100,000/\mu\text{l}$ on day 1 of each cycle in order to proceed with the Paclitaxel infusion. Patients must receive the pre-medication prior to Paclitaxel infusion. If either the granulocyte or platelet count are not adequate, do not continue with treatment. Patients should receive a minimum of 2 cycles unless there is rapid disease progression.

Expected toxicities:

The dose-limiting toxicity of Paclitaxel is neutropenia. Other known toxicities include nausea and vomiting, diarrhea, stomatitis, mucositis, pharyngitis, lymphitis, ischemic colitis, bradycardia, atrial arrhythmia, hypotension, hypertension, sensory (taste), peripheral neuropathy, seizures, mood, hepatic encephalopathy, acute anaphylactoid and urticarial reactions, flushing, rash, pruritis, increased SGOT, SGPT, bilirubin and/or alkaline phosphatase, hepatic failure, hepatic necrosis, alopecia, fatigue, arthralgia, myalgia, light-headedness, myopathy, visual changes (sensation of flashing lights, blurred vision). Local infiltration with Paclitaxel will cause mild local symptoms (erythema, discomfort, induration) that usually resolve within a week. If infiltration occurs, there is the rare possibility of ulceration or rash. Seizure have been reported rarely in association with Paclitaxel use.

Dose Modifications:

Allergic reactions: Patients with grade 1 or 2 allergic reactions may have treatment continued without modifications. Patients with grade 3 or 4 allergic reactions who are responding to treatment may remain on protocol therapy after discussion with Study Chair. Such patients are at risk for recurrent allergic reactions. As a first maneuver, retreatment after premedication with oral recurrent allergic reactions. As a first maneuver, retreatment after premedication with oral dexamethasone 20 mg at 12 and 6 hours pre-administration of Paclitaxel, along with IV H1 and H2-receptor antagonist should be attempted. If necessary, thereafter, infusion rate adjustments will be considered and additional premedications will be administered. These patients must be informed of the potential risks of recurrent allergic reactions and must be carefully monitored.

Hematologic Toxicity: Patients are to be managed as clinically indicated. Colony stimulation factors (G-CSF) should be used in the manner

SiteLongDescription

FastTrack Protocol_INSTANCE_00196 [instance of ManagementTask] - □ ×

ShortDescription
Submit Form C-116

LongDescription
Submit CALGB Advanced Breast Cancer Followup-form (C-116) every two cycles while on protocol therapy, at 6 & 12 months after end of treatment, at disease progression or initiation of non-protocol therapy.

SiteLongDescription
[Empty box]

SiteShortDescription
[Empty box]

FastTrack Protocol Protégé-2000 [C:\My Documents\Latest FastTrack RDF + CALGB 9840\FastTrack Protocol.prf]

Project Edit Window Help

Classes Forms Instances

Relationship: Subclass ▶ V C X

© THING A

- © SYSTEM-CLASS A
- © Diagram_Entity
- © Date
- © ProtocolElement A - 1112
- © EligibilityCriteriaSet - 1124
- © EligibilityCriterion
- © PatientManagementTask - 1130
- © Protocol - 1116
- © ProtocolSchemaDiagram M - 1132
- © Visit - 1128
- © VisitToVisitTransition M - 2210
- © DiseaseArea
- © Am
- © WeightedPath
- © ApplicationArea
- © VisitCycle
- © Disease A
- © DiseaseQualifiers A
- © ModelVersion

1120

1130

1110

© VisitToVisitTransition (instance of Connector_Metaclass)

Name	Constraints	V	C	+	-
VisitToVisitTransition					
Role					
Concrete					

Documentation

A one-way link between a source visit (first_object) and a target visit (second_object). The inherited descriptions specify guidance about when/how/why to make this transition.

Name	Type	Cardinality	Default	Other Facets
first_object	Instance	Single		classes=[Visit]
longDescription	String	Single		
maximumRelativeTime	2218	String	Single	
minimumRelativeTime	2220	String	Single	
preferredRelativeTime	2222	String	Single	
rdfs:isDefinedBy	Instance	Instance	Single	
rdfs:seeAlso	Instance	Instance	Single	
resource_uri	String	Single		
second_object	2216	String	Single	
shortDescription	String	Single		
siteLongDescription	String	Single		
siteShortDescription	String	Single		

Template Slots

Name	Type	Cardinality	Default	Other Facets
first_object	Instance	Single		classes=[Visit]
longDescription	String	Single		
maximumRelativeTime	2218	String	Single	
minimumRelativeTime	2220	String	Single	
preferredRelativeTime	2222	String	Single	
rdfs:isDefinedBy	Instance	Instance	Single	
rdfs:seeAlso	Instance	Instance	Single	
resource_uri	String	Single		
second_object	2216	String	Single	
shortDescription	String	Single		
siteLongDescription	String	Single		
siteShortDescription	String	Single		

First Object Slot Pointer

V	C	+	-
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Rdfs:isDefinedBy

V	C	+	-
---	---	---	---

Rdfs:seeAlso

V	C	+	-
---	---	---	---

Second Object Slot Pointer

V	C	+	-
---	---	---	---

Superclasses

+	-
---	---

© Transition A M

23/41

1818

FastTrack Protocol_INSTANCE_00023 [instance of VisitToVisit Transition]

ShortDescription	PreferredRelativeTime
Arm A Treatment to Arm A Treatment Retry #	7
First Object	MaximumRelativeTime
V C + -	7
Arm A Treatment Visit	MinimumRelativeTime
Second Object	7
V C + -	7
Arm A Treatment Retry #1	
LongDescription	
If either granulocyte or platelet count are not adequate, blood counts should be repeated weekly and treatment should be instituted when there has been hematologic recovery. Patients receiving G-CSF are not eligible for re-treatment unless they have been off G-CSF for a minimum of 24 hours.	
SiteLongDescription	<input checked="" type="checkbox"/> IsPreferredTransition
	2310
SiteShortDescription	

FIG. 23

FastTrack Protocol Protégé-2000 [C:\My Documents\Latest\FastTrack RDF + CALGB 9840\FastTrack Protocol.prt]

Project Edit Window Help

Classes Forms Instances

Relationship: Subclass ▶ V C X

© C :THINGA

- o C :SYSTEM-CLASSA
- o Diagram_Entity
- o Date
- o ProtocolElementA — 1112
- o EligibilityCriteriaSet — 1124
- o EligibilityCriterion
- 1125 C:PatientManagementTask — 1130
- 1126 C:Protocol — 1116
- 1127 C:ProtocolSchemaDiagram — 1132
- 1128 C:Visit — 1128
- 1129 C:VisitToVisitTransition — 2210
- 1130 C:DiseaseArea
- 1131 C:AM
 - o C:WeightedPath
 - o ApplicationArea
 - o VisitCycle
 - o DiseaseA
 - o DiseaseQualifiersA
 - o ModelVersion

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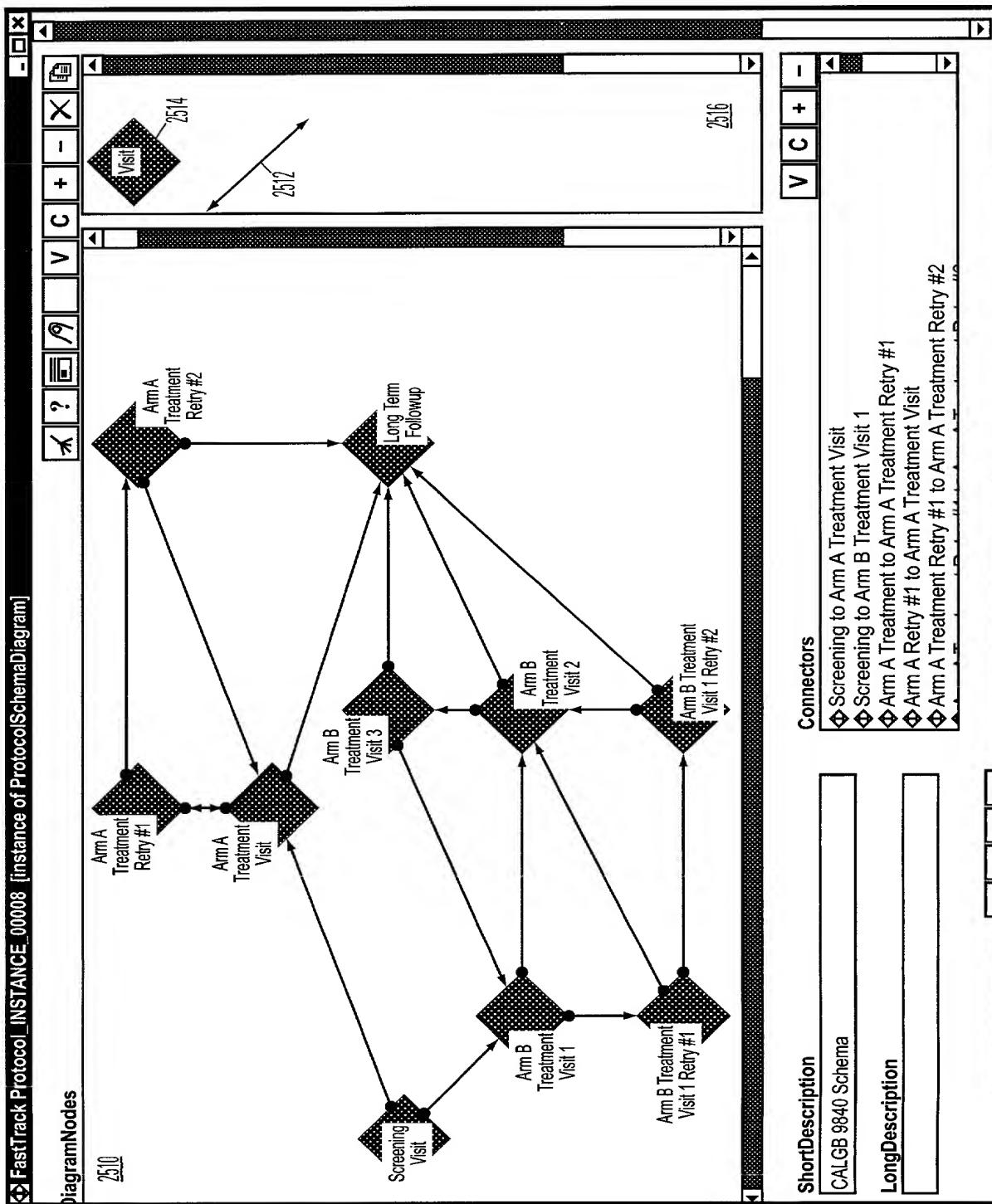


FIG. 25

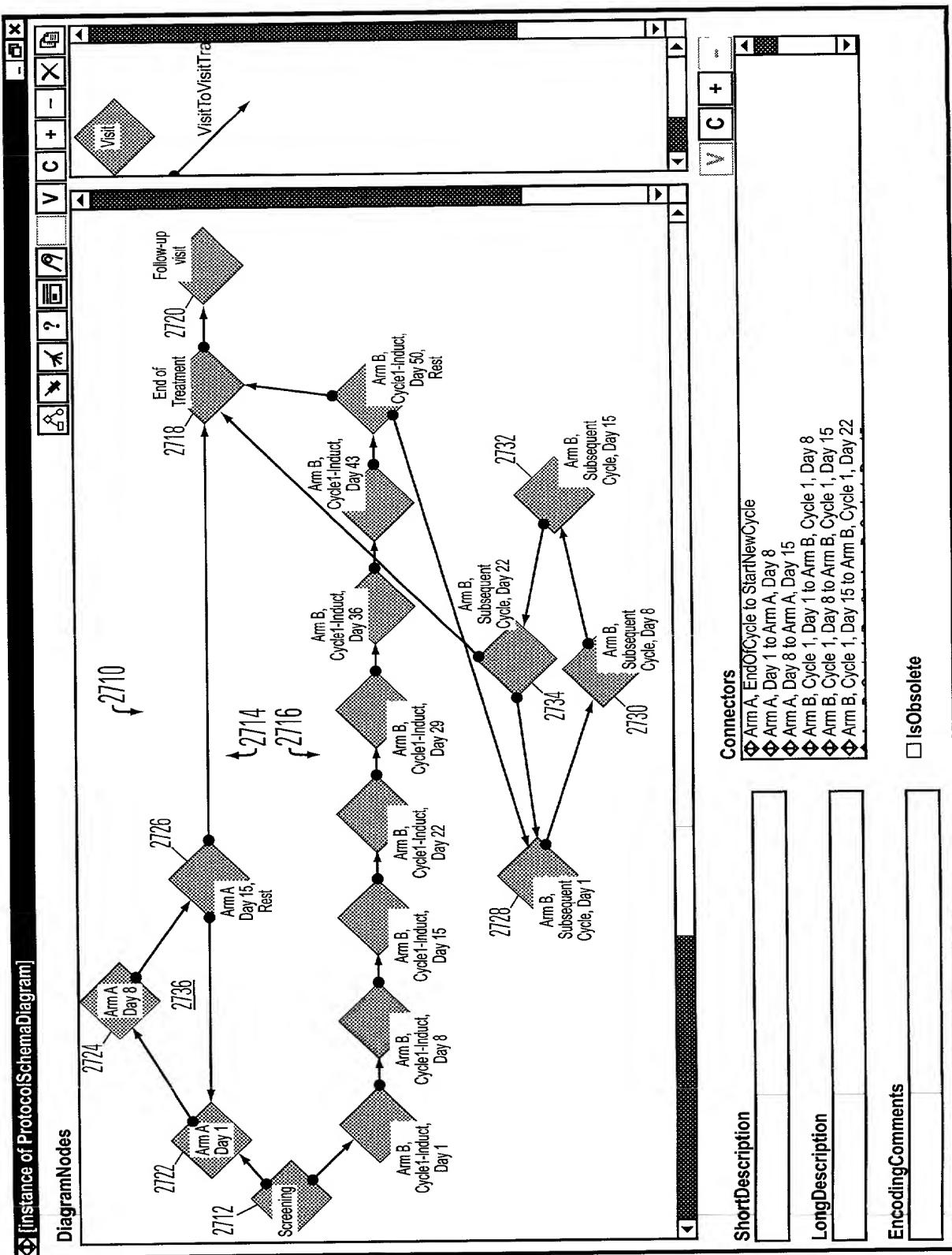
26/41

940

© DisambiguationComment

Name	Documentation	Constraints	
DisambiguationComment			
Role			
Concrete			
Template Slots			
Name	Type	Cardinality	Other Facets
2610 [S] conceptualProtocolSection	Symbol	multiple	allowed-values={Protocol Summary,...
2612 [S] documentReferences	Instance	multiple	classes={DocumentReference}
2614 [S] Impact Type	Symbol	multiple	allowed-values={Safety,Efficacy-prim..
2616 [S] Issue	String	single	
2618 [S] Potential Impact	String	single	
2620 [S] Protocol text	String	single	
2622 [S] Recommendation	String	single	
2624 [S] Severity Level	Symbol	single	allowed-values={Level One,LevenTw..
2626 [S] Short Description	String	single	

FIG. 26



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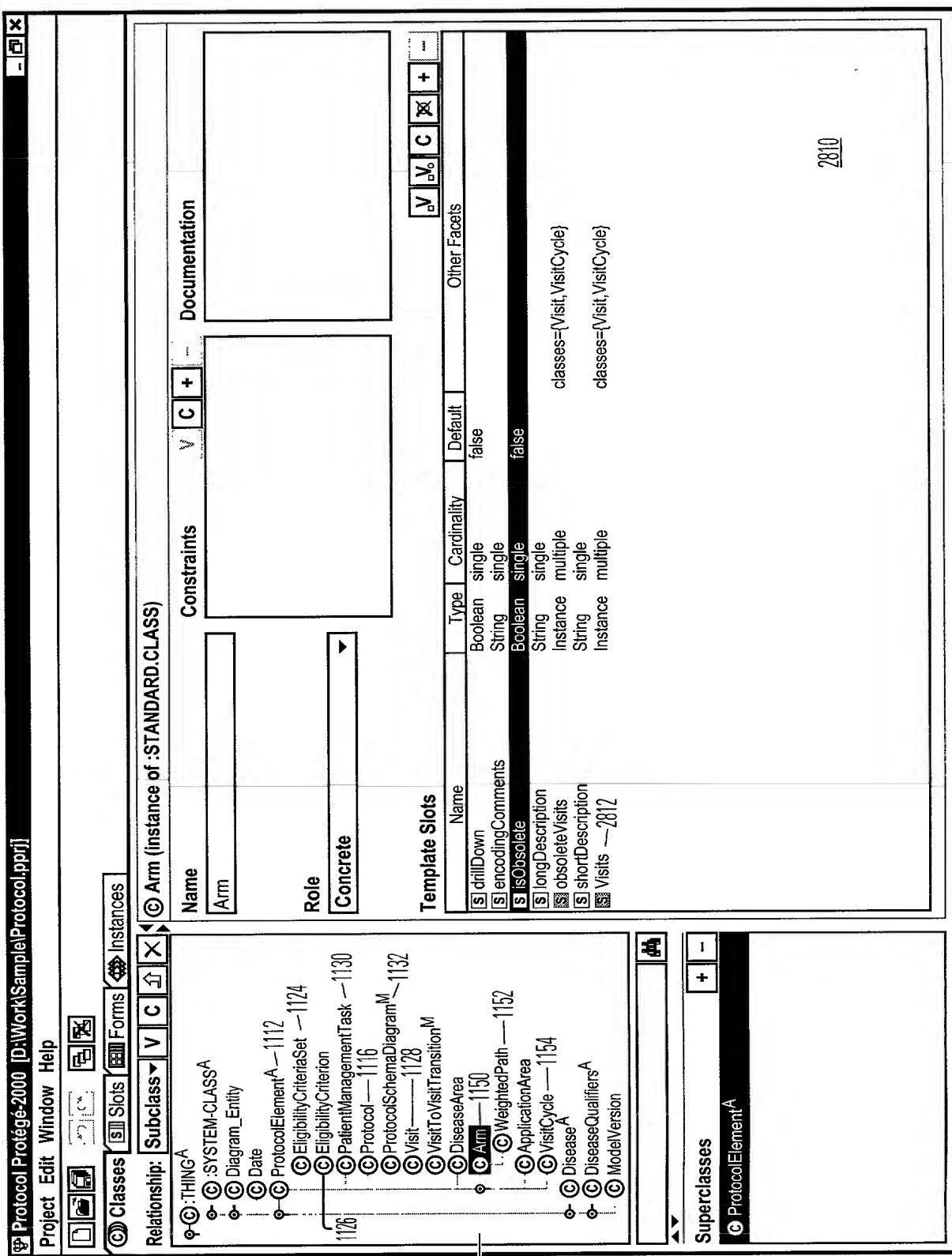
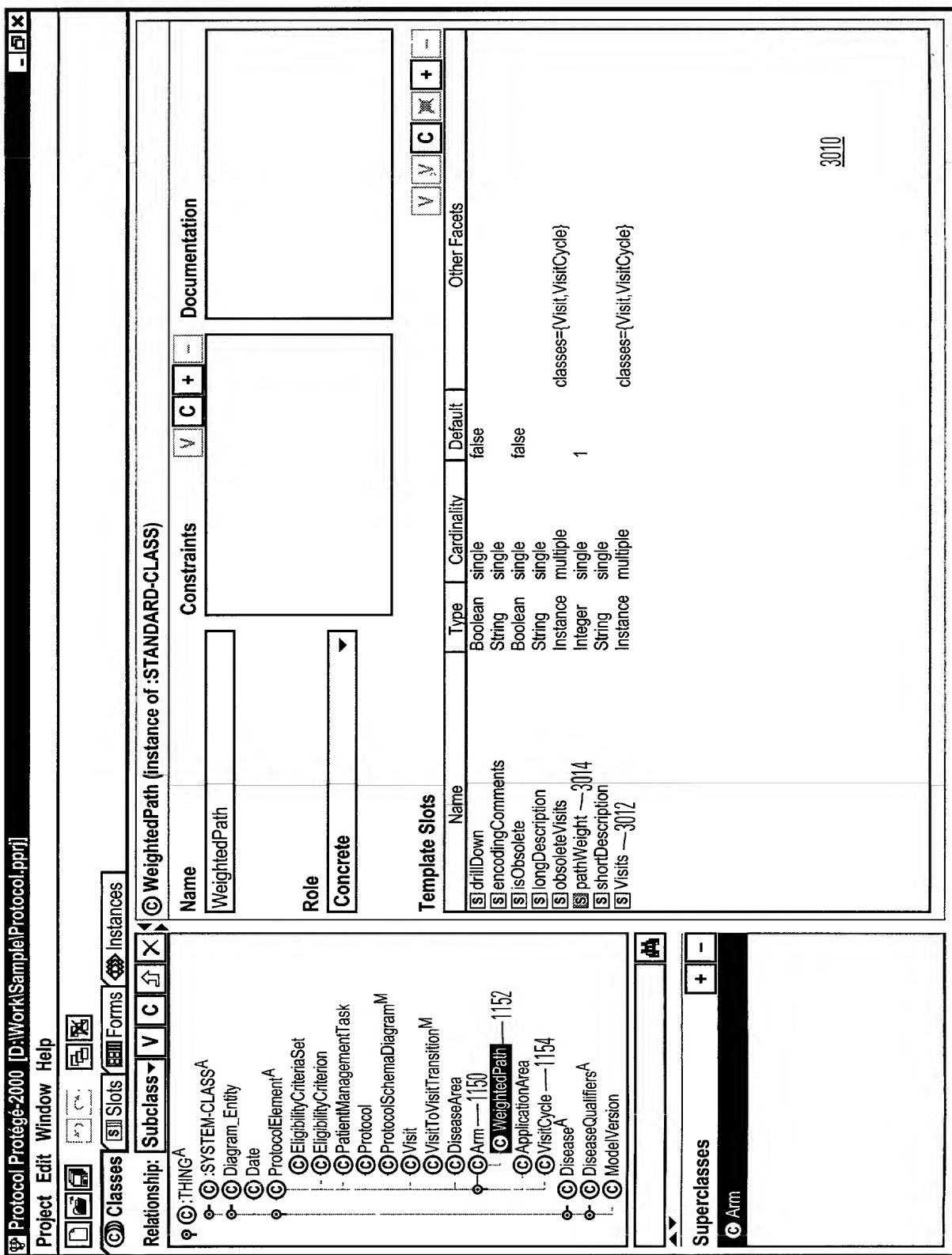


FIG. 28

Instance of Arm

ShortDescription Arm A → 2710	EncodingComments Editorial change
LongDescription Arm A: Gemcitabine and Irinotecan HCl (CPT-11)	
Visits V C + ... ◆ Screening → 2712 ◆ Arm A, Day 1 → 2722 ◆ Arm A, Day 8 → 2724 ◆ Arm A, Day 15, Rest → 2726 ◆ End of Treatment → 2718 ◆ Follow-up Visit → 2720	ObsoleteVisits V C + ...
<input type="checkbox"/> IsObsolete <input type="checkbox"/> DrillDown	



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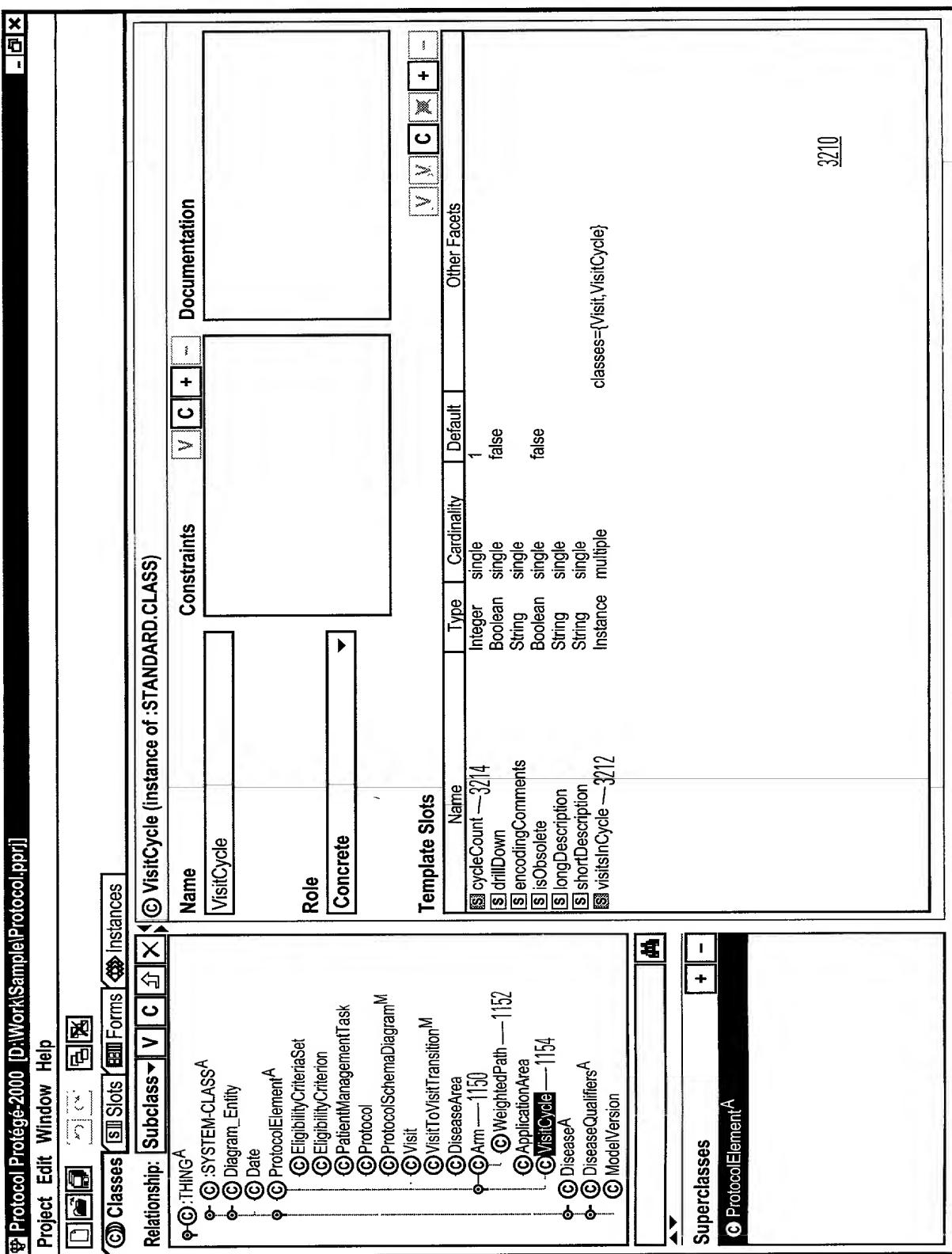
3110

Instance of WeightedPath

ShortDescription	Visits
Arm A Path	◆ Screening ← 2712 ◆ Arm A Cycle ← 2736 ◆ End of Treatment ← 2718 ◆ Follow-up cycle ← 2720
LongDescription	
EncodingComments	PathWeight
	1
<input type="checkbox"/> IsObsolete	<input type="checkbox"/> DrillDown

FIG. 31

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3210

FIG. 32

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2736

□ [instance of VisitCycle]

ShortDescription Arm A Cycle	VisitsInCycle V C + - ◆ Arm A, Day 1 ← 2722 ◆ Arm A, Day 8 ← 2724 ◆ Arm A, Day 15, Rest ← 2726
LongDescription 	
EncodingComments 	CycleCount 3
<input type="checkbox"/> DrillDown	<input type="checkbox"/> IsObsolete

FIG. 33

 Lack of specific bounds on 1st MSFC relative to Randomization (DisambiguationComment)

ShortDescription
Lack of specific bounds on 1st MSFC relative to Randomization

NOTE to ANALYSTS: please assoc text w/ each DocReference PRN

ConceptualProtocolSection

Timing of Events
Screening Assessments
Study Flow Chart

DocumentReferences

◇ 32
◇ 31

Potential Impact
The time window around the first practice test for MSFC really must happen at least 11 days before randomization, in order for the next two tests to occur at least 5 days apart from each other. This upper bound on the time window is not specified.

Impact Type
Efficacy-primary

Recommendation
Change "(Within 35 days of randomization)" for first practice test (MSFC) to say "(Between 35 and 11 days of randomization.)."

⊕ Inconsistent tasks in tx plan and assessment table (DisambiguationComment)

ShortDescription Inconsistent tasks in tx plan and assessment table	Severity Level Level One	Document Page p. 13, p. 31
Protocol Text "b) Baseline safety evaluation --- laboratory tests 2 days following the first infusion will include: ionized calcium, magnesium, phosphorus, creatinine, and CBC..."	Additional reference comments	
Issue The assessment schedule on page 31 does not list the creatinine.	Protocol Section Treatment Plan Schedule of Events	Impact Type Safety
Potential Impact A safety assessment could be missed, having the potential impact of missing the timely deflection of an adverse event.		
Recommendation Add in the creatinine task to the assessment summary.		

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3610

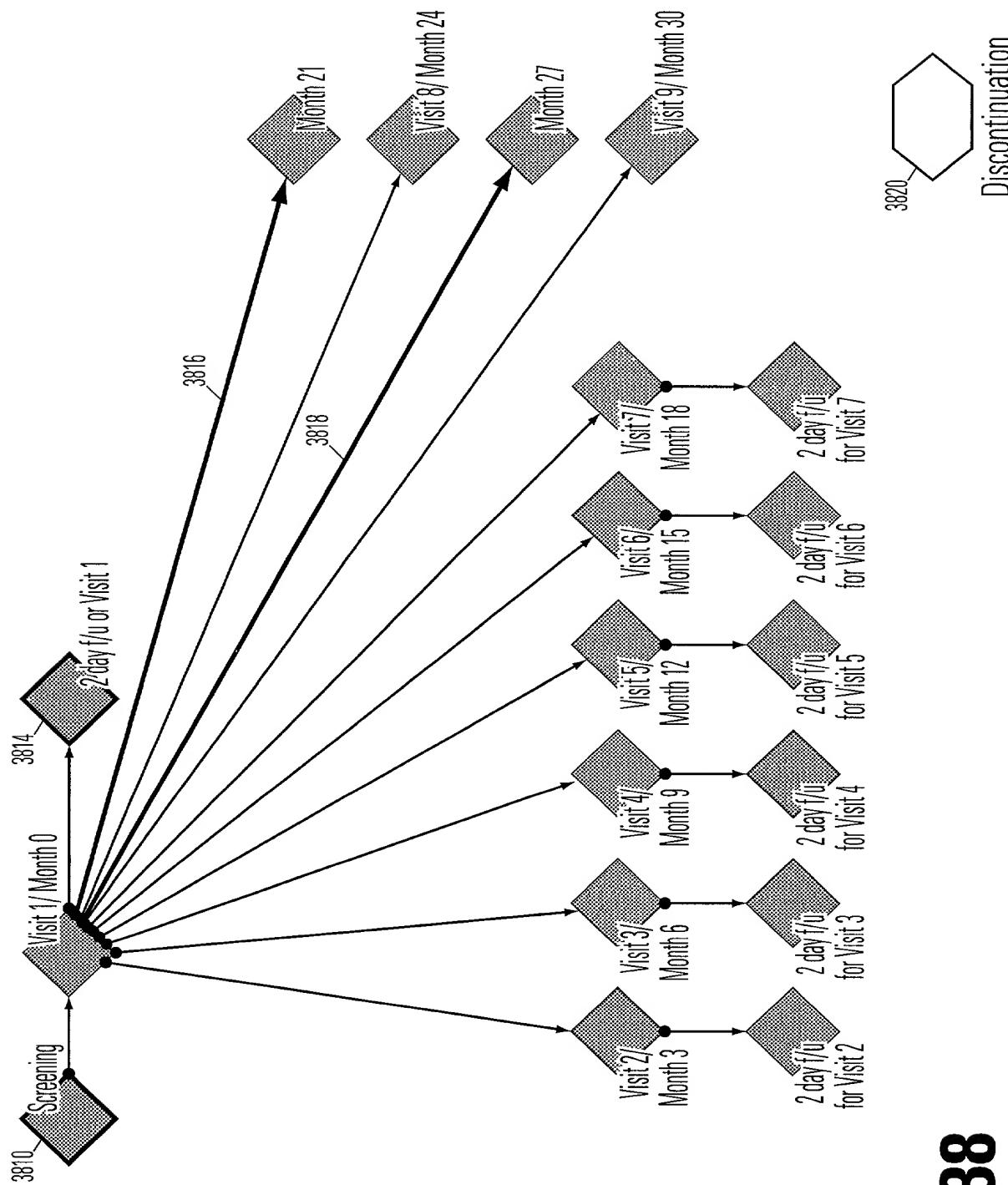
© DocumentReference

Name	Documentation	Constraints	
DocumentReference		V C + -	
Role			
Concrete			
Template Slots			
Name	Type	Cardinality	Other Facets
S addDocRefInfo	String	single	
S disambiguationComments	Instance	multiple	classes={DisambiguationComment}
S drillDown	Boolean	single	default={false}
S encodingComments	String	single	
S literalSponsorSectionName	String	single	
S longDescription	String	single	
S pageNumber	String	single	
S protocolText	String	single	
S sectionReferenceNumber	String	single	
S shortDescription	String	required single	

FIG. 36

31 (Document Reference)

PageNumber 31	SectionReferenceNumber 11.1.2
LiteralSponsorSectionName VisualFunction and MSFC Practice Tests	AddlDocRefInfo Examining Technician instructions
ProtocolText "...performed three times within 35 days prior to randomization, with at least 5 days between any two evaluations.."	
EncodingComments	



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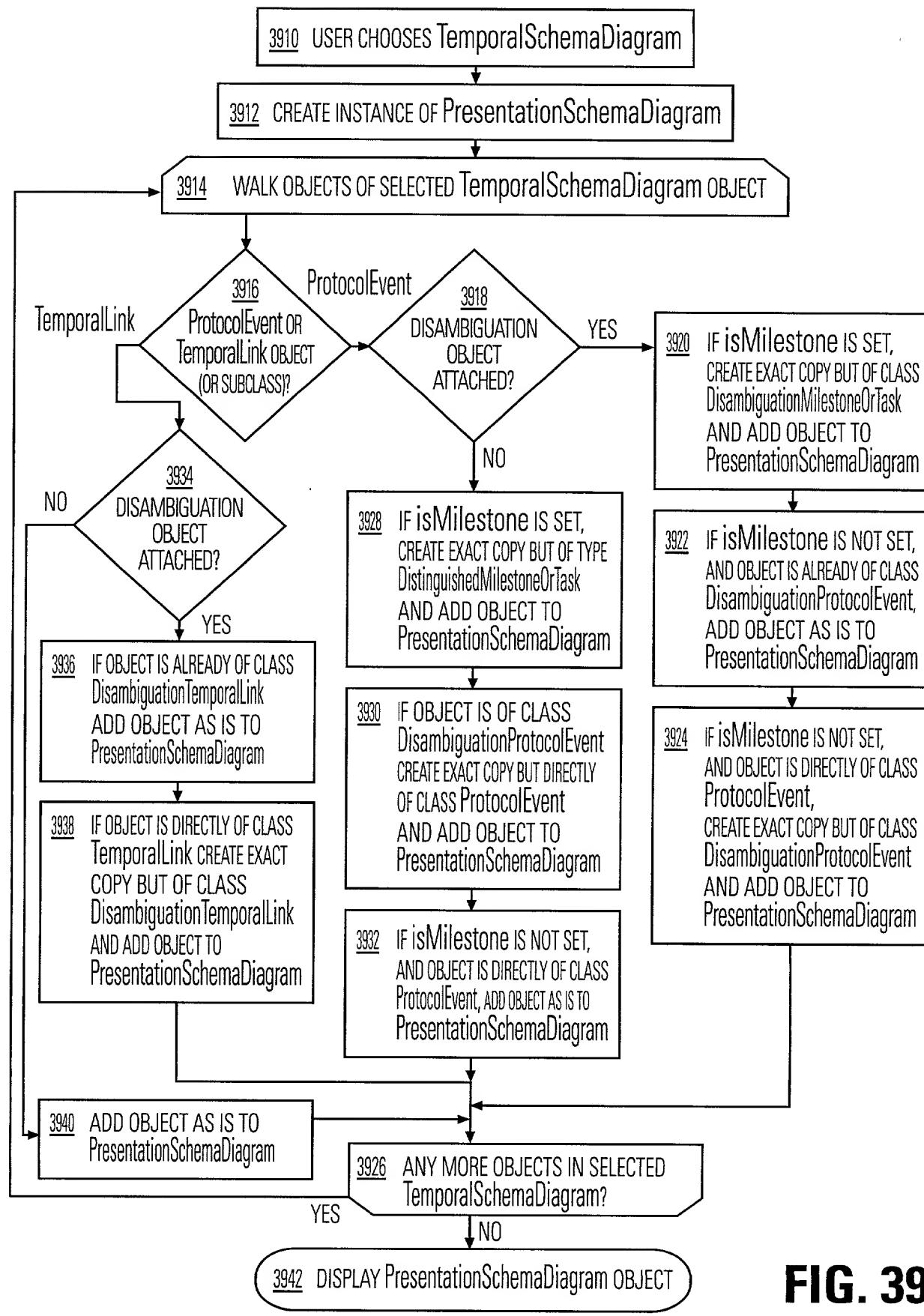


FIG. 39

DISAMBIGUATION FINDINGS

Item	Impact Type	Protocol Section	Description	Document Reference
1	Safety Efficacy-primary Efficacy-secondary	Protocol Summary Study Flow Chart	<p>Issue: The description in the Protocol Synopsis of when assessments should be performed after 16 weeks is not consistent with Appendix I Schedule of Assessments.</p> <p>Potential Impact: Confusion as to when to perform these evaluations (clinical parameters and safety assessments) could result in inconsistent and inaccurate collection of data for the study.</p> <p>Recommendation: Revise sentence in the Protocol Synopsis to read, "After 16 weeks these evaluations will be performed every two to "four" months..." in order to be consistent with the timepoints indicated in Appendix I Schedule of Assessments.</p>	<p><i>Pg. 12; Section Protocol Synopsis; Procedure; Paragraph 6:</i> "Clinical parameters (ACR core set) and safety assessments (adverse events and laboratory parameters) will be performed at baseline and then at monthly intervals up to 16 weeks. After 16 weeks these evaluations will be performed every two to three months, up to 104 weeks."</p>

Item	Impact Type	Protocol Section	Description	Document Reference
4	Safety Accrual	Screening Assessments Study Flow Chart	<p>Issue: The protocol text specifies that if an analysis with evidence of seropositivity was performed within 6 months before screening, then rheumatoid factor testing will not have to be performed at screening. However, this is not noted in Appendix I Schedule of Assessments.</p> <p>Potential Impact: Unnecessary analysis performed at screening.</p> <p>Recommendation: Add a footnote to the Rheumatoid Factor assessment in Appendix I to clarify that documented evidence of seropositivity is acceptable as screening data if obtained within 6 months before screening.</p>	<p><i>Pg. 28; Section 8.6.2; Rheumatoid Factor: "Unless there is documented evidence of rheumatoid factor titre within 6 months before screening a blood sample for this analysis will be taken."</i></p> <p><i>Pg. 41; Section Appendix I; Schedule of Assessments</i></p>